10/629,022

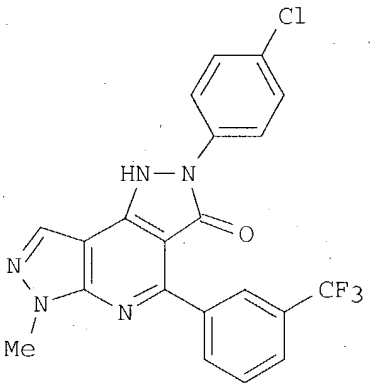
STN Structure Search
2.26.04

=> d ibib abs hitstr

Inventors

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:427773 CAPLUS
DOCUMENT NUMBER: 140:42073
TITLE: Structure-activity studies of a series of dipyrazolo[3,4-b:3',4'-d]pyridin-3-ones binding to the immune regulatory protein B7.1
AUTHOR(S): Green, Neal J.; Xiang, Jason; Chen, Jing; Chen, Lihren; Davies, Audrey M.; Erbe, Dave; Tam, Steve; Tobin, James F.
CORPORATE SOURCE: Department of Chemical Sciences, Wyeth Research, Cambridge, MA, 02140, USA
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(13), 2991-3013
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

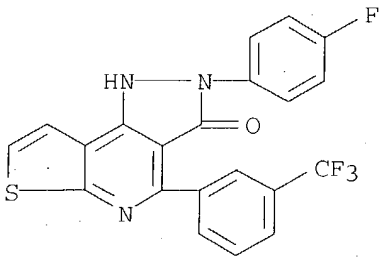


I

AB The interaction of co-stimulatory mols. on T cells with B7 mols. on antigen presenting cells plays an important role in the activation of naive T cells. Consequently, agents that disrupt these interactions should have applications in treatment of transplant rejection as well as autoimmune diseases. To this end, specific small mol. inhibitors of human B7.1 were identified and characterized. Herein, we report the identification of potent small mol. inhibitors of the B7.1-CD28 interaction. In a high-throughput screen we identified several leads that prevented the interaction of B7.1 with CD28 with activities in the nanomolar to low micromolar range. One of these, the dihydrodipyrazolopyridinone I, was subsequently shown to bind the V-like domain of human B7.1 at equimolar stoichiometry. With this as a starting point, we report here the synthesis and initial in vitro structure-activity relationships of a series of these compds.

IT **635325-26-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationship of a series of dipyrazolo[3,4-b:3',4'-d]pyridin-3-ones as inhibitors of the B7.1-CD28 interaction in T cells)

RN 635325-26-7 CAPLUS
CN 3H-Pyrazolo[3,4-d]thieno[2,3-b]pyridin-3-one, 2-(4-fluorophenyl)-1,2-dihydro-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'CAPLUS' ENTERED AT 17:06:15 ON 26 FEB 2004
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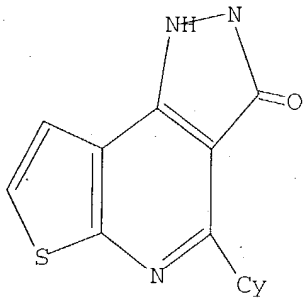

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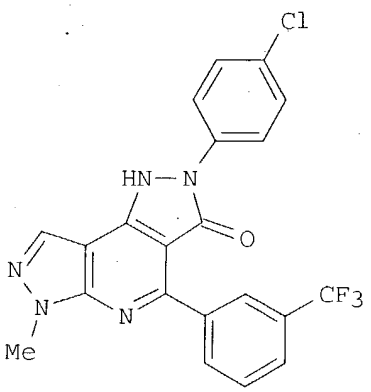
L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:427773 CAPLUS
DOCUMENT NUMBER: 140:42073
TITLE: Structure-activity studies of a series of dipyrazolo[3,4-b:3',4'-d]pyridin-3-ones binding to the immune regulatory protein B7.1
AUTHOR(S): Green, Neal J.; Xiang, Jason; Chen, Jing; Chen, Lihren; Davies, Audrey M.; Erbe, Dave; Tam, Steve; Tobin, James F.
CORPORATE SOURCE: Department of Chemical Sciences, Wyeth Research, Cambridge, MA, 02140, USA
SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(13),

2991-3013
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



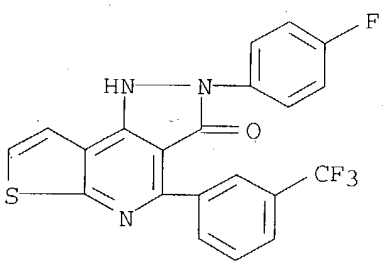
I

AB The interaction of co-stimulatory mols. on T cells with B7 mols. on antigen presenting cells plays an important role in the activation of naive T cells. Consequently, agents that disrupt these interactions should have applications in treatment of transplant rejection as well as autoimmune diseases. To this end, specific small mol. inhibitors of human B7.1 were identified and characterized. Herein, we report the identification of potent small mol. inhibitors of the B7.1-CD28 interaction. In a high-throughput screen we identified several leads that prevented the interaction of B7.1 with CD28 with activities in the nanomolar to low micromolar range. One of these, the dihydrodipyrazolopyridinone I, was subsequently shown to bind the V-like domain of human B7.1 at equimolar stoichiometry. With this as a starting point, we report here the synthesis and initial in vitro structure-activity relationships of a series of these compds.

IT **635325-26-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity relationship of a series of dipyrazolo[3,4-b:3',4'-d]pyridin-3-ones as inhibitors of the B7.1-CD28 interaction in T cells)

RN 635325-26-7 CAPLUS

CN 3H-Pyrazolo[3,4-d]thieno[2,3-b]pyridin-3-one, 2-(4-fluorophenyl)-1,2-dihydro-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



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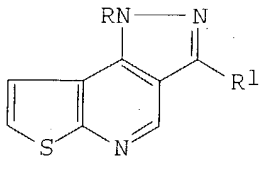
L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:438409 CAPLUS
DOCUMENT NUMBER: 99:38409
TITLE: 1H-Pyrazolo[3,4-d]thieno[2,3-b]pyridine and its derivatives
AUTHOR(S): Khan, Misbahul Ain; Rolim, Alice Maria Coimbra; Guarconi, Antonio Elydio
CORPORATE SOURCE: Sec. Quim., Inst. Mil. Eng., Rio de Janeiro, 22290, Brazil
SOURCE: Journal of Heterocyclic Chemistry (1983), 20(2), 475-6
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 99:38409
GI



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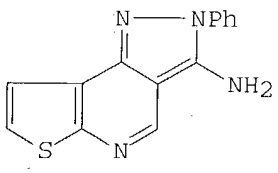

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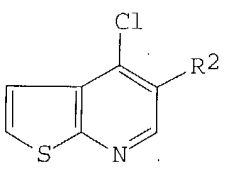
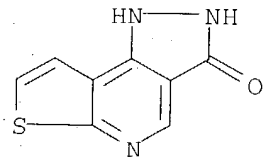


V

AB Title compds. I [R, R1 = H, NH2 (II); H, OH (III); Me, NH2; H, H; H, Br; Ac, NHAc] and IV were prepared E.g., refluxing thienopyridine V (R2 = CN, CO2Et) with N2H4 gave 75% II and 80% III resp.

IT **63873-63-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 63873-63-2 CAPLUS
CN 3H-Pyrazolo[3,4-d]thieno[2,3-b]pyridin-3-one, 1,2-dihydro- (9CI) (CA INDEX NAME)



L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:502223 CAPLUS
DOCUMENT NUMBER: 87:102223
TITLE: The synthesis of thieno[3,2-e]pyrazolo[4,3-c]pyridine. A new heterocyclic system
AUTHOR(S): Khan, Misbahul; Guarconi, Antonio Elydio
CORPORATE SOURCE: Secao Quim., Inst. Mil. Eng., Rio de Janeiro, Brazil
SOURCE: Heterocycles (1977), 6(6), 727-9
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 87:102223

10/629,022

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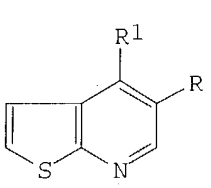

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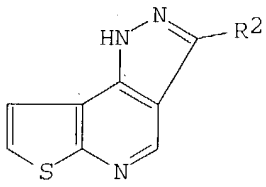


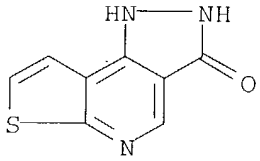
II

AB Reaction of thienopyridine I (R = CN, CO2Et; R1 = OH) with POCl3 gave 76% I (R1 = Cl). Treatment of I (R = CN, R1 = Cl) with N2H4 under reflux gave 85% II (R2 = NH2); II (R2 = OH) was prepared similarly in 80% yield from I (R = CO2Et, R1 = Cl).

IT **63873-63-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 63873-63-2 CAPLUS

CN 3H-Pyrazolo[3,4-d]thieno[2,3-b]pyridin-3-one, 1,2-dihydro- (9CI) (CA INDEX NAME)



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L7 2 S L5 FULL

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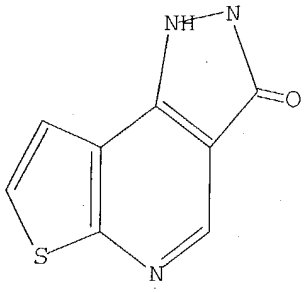

Structure attributes must be viewed using STN Express query preparation.

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PALM INTRANET

Day : Thursday
Date: 2/26/2004
Time: 17:12:42

Inventor Name Search Result

Your Search was:

Last Name = GREEN
First Name = NEAL

Application#	Patent#	Status	Date Filed	Title
60490713	Not Issued	020	07/28/2003	ELECTRONIC CIRCUIT BUILDING BLOCK
60399225	Not Issued	159	07/29/2002	DIHYDROPYRAZOLO[3,4-D]THIENO-[2,3-B]PYRIDIN INHIBITORS OF B7-1.
60399161	Not Issued	159	07/29/2002	DIHYDRODIPYRAZOLOPYRIDINONE INHIBITORS O B7-1
60399146	Not Issued	159	07/29/2002	DIHYDRODIPYRAZOLOPYRIDINYLBENZAMIDE AN -SULFONAMIDE INHIBITORS OF B7-1
10629276	Not Issued	094	07/28/2003	DIHYDRODIPYRAZOLOPYRIDINYLBENZAMIDE AN -SULFONAMIDE INHIBITORS OF B7-1
10629227	Not Issued	030	07/28/2003	DIHYDRODIPYRAZOLOPYRIDINONE INHIBITORS O B7-1
10629022	Not Issued	030	07/28/2003	DIHYDROPYRAZOLO[3,4-D]THIENO-[2,3-B]PYRIDIN INHIBITORS OF B7-1

Inventor Search Completed: No Records to Display.

Search Another: Inventor

Last Name Green **First Name** Neal

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